MINUTES OF THE MEETING OF THE TASK FORCE EXAMINING HORMONE REPLACEMENT THERAPY

227 French Landing Poplar Room
Heritage Place Metro Center
Nashville, TN 37243

December 16, 2011

MINUTES

Call to Order: Keith Lovelady, MD called the meeting to order at 9:00 a.m.

Members Present: Keith Lovelady, MD, Cheryl Stegbauer, PH.D, APN, RN, Karen Shepherd, DO and Johnny Nowlin, PA-C.

Staff Present: Elizabeth Lund, Executive Director, Board of Nursing, Rosemarie Otto, Executive Director, Board of Medical Examiners, and Andrea Huddleston, Deputy General Counsel.

Discussion: A roll call was taken to identify for the record members present. Dr. Lovelady agreed to chair the meeting. Ms. Huddleston outlined House Joint Resolution 104 which requires the board of medical examiners, in collaboration with the board of nursing and the committee on physician assistants, to study and to recommend a standard of care for hormone replacement therapy and the promulgation rules addressing any identified deficiencies in the oversight or delivery of such therapy. The study should give consideration to, but not be limited to, advertising claims by health care provides who deliver hormone replacement therapy, the qualifications of the medical directors involved in delivery of hormone replacement therapy, and the qualifications and supervision of allied health care providers offering hormone replacement therapy. The board of medical examiners, in collaboration with the board of nursing and the committee on physician assistants, must complete its study and report its findings, recommendations, and any proposed rules and legislation to the house health and human resources committee and the senate general welfare, health and human resources committee on or before January 31, 2012. Dr. Lovelady read the most salient portions of the resolution into the record for the benefit of those in the audience.

The Task Force heard from Ms. Laurie Tompkins, APN. Ms. Tompkins is a woman's health advanced practice nurse who practices at Vanderbilt University's Women's Health Center. Ms. Tompkins provided the Task Force with five case studies of patients she has seen in her office who presented with various complaints following the initiation of hormone replacement therapy in pellet form.

Patient AC presented with vaginal bleeding at 57 years of age and 5 years post menopausal of 1 month duration. She had been using pellets for 6 months. E and T implants and progesterone troche at bedtime. Her workup included Labs, PUS which showed endometrial thickness to be 8mm. An endometrial biopsy followed. Results: Hct. 37%, Serum testosterone 6 x normal, Serum estradiol 101mg/dl, Serum progesterone 0.8mg/dl. EMB benign hyperplasia. Patient is managed now with oral iron therapy, aygestin 5 mg daily for 90 days. Patient AC followed up with Ms. Tompkins 90 days later and her endometrial thickness was reduced to 3-4 mm. Repeat EMB 90 days benign endometrial tissue. Follow up in 3 months recommended at which time she returned with menopausal symptoms but no bleeding. Workup repeated with PUS only, and her endometrial thickness normal. The

patient was started on transdermal estradiol and prometrium. Patient AC has done well since.

Patient SB presented with post menopausal vaginal bleeding of 2 weeks at 61 years of age. She had been on hormone therapy for menopause sxs for 4 years without problems, changed to pellets for the last year. Patient began to bleed heavily and experienced significant cramping. E and T implants. The patient was given a prescription for oral progesterone which she took daily. Initial workup included endometrial biopsy, CBC, hormone levels. Findings were serum estradiol 161mg/dl, serum testosterone 2 x normal, serum progesterone 1.0mg/dl. PUS showed endometrial thickness to be 6-7 mm with small mass with feeder vessel consistent with an endometrial polyp. EMB was benign inflammatory. Patient was placed on a trial of aygestin which did not resolve her bleeding. Hysteroscopic examination showed an endometrial polyp that was removed and pathology was benign. Follow up has been uneventful.

Patient MM is 54 years of age and presented with post menopausal vaginal bleeding. Patient has a history of endometrial hyperplasia with D&C evaluation 3 years ago. Patient MM had been followed with annual PUS which was normal. Patient MM had not been seen for one year during which time she began pellet therapy with E and T and troche progesterone. Patient MM's additional complaints included acne, hirsutism and vocal changes. Ms. Tompkins' workup of Patient MM included labs, PUS and endometrial biopsy. The results revealed mild anemia and benign hyperplasia. With hyperplasia diagnosis patient elected to undergo a laparoscopic supracervical hysterectomy and has done well. Her skin changes have resolved, the vocal changes have been evaluated and she has been advised, this might improve slightly, but the soft tissue changes are probably permanent.

Patient JS is 57 years old who presented with anxiety and depression and hot flashes. Post hysterectomy and bilateral salpingoophorectomy in her late 40's. The patient was using pellets with testosterone only. Patient JS is 5 year breast cancer survivor and had been advised not to use estrogen therapy. She had not been treated with aromatase inhibitors. She had no pre-existing history of depression or anxiety. Her labs were initially evaluated and found a serum estradiol of 75ng/dl. Testosterone level was 1300 ng/dl (normal for a male is 300-1200, Female levels recommended at 30-95ng/dl). She also had significant clitoral hypertrophy, typical male pattern baldness, acne and severe anxiety. Ms. Tompkins work up of the patient included a consultation with a breast center and oncology. Ultimately, she was placed on two separate anti-anxiety/anti-depressant medications. She continues on the SSRI and has been weaned off her anti-anxiety medication. Her Labs were checked monthly to monitor and her estradiol levels which were back to normal expected values (<20ng/dl) at 5 months post her last testosterone implant insertion. Patient at 7 months now and her most recent testosterone level was 180ng/dl -– still double the recommended female levels.

Patient JW is 49 years old and presented with menorrhagia. Patient entered menopause at the age of 44. She had no hormone therapy until 48 yrs. Patient JW has been on pellets for one year. She presented with heavy uterine bleeding for 4 weeks. Mr. Tompkins' initial workup of Patient JW included labs, PUS, and an EMB. The results revealed HCT 24% - severe blood loss anemia, PUS showed endometrial thickness of 1.2cm's. EMB showed hyperplasia with atypia. She is a flight attendant and was advised that flying would be dangerous with such severe anemia and was placed on sick leave for 2 weeks. She was unable to take off any additional time from work for surgery and was therefore managed with oral aygestin for 90 days and oral iron. Bleeding resolved and HCT was normal at 90 day follow up. Repeat PUS showed endometrial thickness at 6mm. Repeat biopsy shows simple hyperplasia without atypia. Patient JW continues on a aygestin and will follow up in 3

more months. Hysterectomy has been recommended. She is a single mom with a high deductible insurance plan and cannot take off work to have surgery.

Ms. Tompkins pointed out that many patients are not being thoroughly worked up prior to the initiation of treatment with hormone replacement pellets and that many of the patients believe that simply because the pellet treatment is advertised as "natural" there are no side effects or consequence. She believes that patients are not properly educated by providers about the risks and benefits of the use of pellets prior to the initiation of pellet hormone replacement therapy. Additionally, Ms. Tompkins cited the lack of medical supervision of the patient after pellet therapy begins; patients with complications are not managed but are instead referred for gynecological care elsewhere.

The Task Force identified several major issues which include: First, there is a knowledge deficit among the patients; they simply do not know the risks and benefits of pellet hormone replacement therapy. Second, there maybe a deficit in medical decision making such as whether this treatment is appropriate for the particular patient. Third, there must be adequate medical supervision and care of the patient which includes an evaluation and development of a treatment plan that includes appropriate follow up. Third, pellets are being implanted and the question arises whether or not this is in the providers' scope of practice. It was pointed out that there is a difference between a patient who goes to a compounding pharmacy with a prescription in hand for a hormone from a provider and the clinic actually dispensing the pellet themselves. In the case of the former, there is an assumption that an appropriate examination and work up has been done by the provider. In the case of the later, no such assumption can be made.

There was a discussion about the lack of reliable studies on the use of pellets for hormone replacement therapy.

The Task Force reviewed the Opinion 322 of the American College of Gynecologists entitled "*Compounded Bioidentical Hormones*". The *Abstract* provides that "[C]ompounded bioidentical hormones are plant-derived hormones that are prepared, mixed, assembled, packaged, or labeled as a drug by a pharmacist and can be custom made for a patient according to a physician's specifications. Most compounded products have not undergone rigorous clinical testing for safety or efficacy, and issues regarding purity, potency, and quality are a concern. Compounded hormone products have the same safety issues as those associated with hormone therapy agents that are approved by the US Food and Drug Administration and may have additional risks intrinsic to compounding. There is no scientific evidence to support claims of increased efficacy or safety for individualized estrogen or progesterone regimens."

The Task Force heard from several members of the audience all of whom expressed their appreciation for the work on the Task Force, but spoke in support of the use of hormone replacement pellets.

Morgan Moore, MD spoke on behalf of the use of pellets in hormone replacement therapy. She invited "each and everyone" to come to her office for a day to observe how her practice takes care of patients. She believes that her practice adheres to an acceptable standard of care and that her patients are well advised about the risks and benefits of the use of pellets in hormone replacement therapy. In her clinic nurses are not allowed to prescribe. Moreover, patients are advised to have regular gynecological examinations which include pelvic and breast examinations. Additionally, lab work is done on all patients prior to the initiation of pellet therapy. Patients are required to return to the office for follow up care as well. Dr. Moore said that she now does pelvic and breast examinations for her patients

because she said that many of her patients "get flack" from their other providers when they learn that patient in on pellet therapy. She believes that there is a lack of knowledge among the state's physicians and other providers regarding hormone replacement therapy.

Mr. Mark Binkley, Pharm. D Dr. Binkley spoke to the Task Force from the compounding pharmacy perspective on the use of pellet hormone replacement therapy. Compounding is versatile and allows for individualized therapy based on a prescription. Mr. Binkley urged the Task Force not to "throw the baby out with the bath water." The use of pellets is effective when prescribed properly but it is incumbent upon the provider to insure that the patient is appropriately worked up and followed throughout the treatment.

Mr. John Hollis, Pharm. D Dr. Hollis, a compounding pharmacist spoke to the Task Force next. He has been compounding pellets for 10-15 years. He informed the Task Force that pellets were on the market some years ago but were taken off the market. His pharmacy uses approved pharmaceutical ingredients. Dr. Hollis frequently attends compounding meetings and believes that a patient can be harmed by an FDA-approved product as well as anything he compounds. Dr. Hollis gets a prescription for everything he does. According to Dr. Hollis, he is an expert at making the medication not an expert at using the medication. He too urged the Task Force "not to throw the baby out with the bath water." He believes that compounding pellets are the most effective way to deliver hormone replacement therapy.

Ms. Cindy Smith, Pharm. D. Dr. Smith has been providing bioidentical services in conjunction with physicians since 2003. She does not actually use pellets. She uses topical replacement products. She indicated that she spends approximately 45 minutes to an hour with each patient and informs them of the risks and benefits of compounding bioidenticals. She does follow up with the patient. She does not do physical examinations, but follows up to insure that the patient is getting regular pelvic and breast examinations. They have seen over 6,000 patients that they compound for since 2003. She is unaware of any breast cancers or endometrial cancers. In her practice, approximately 1,100 compounds are prepared per month. In her practice, she works with physicians but actually develops the dosing amount after consultation with the patient and then provides it to the physician who "signs off on it."

The Task Force asked for additional information from staff including what other states may be doing on this issue. The Task Force will meet again the second week of January 2012 to here additional information and to prepare a response to House Joint Resolution 104.

These minutes were ratified by the Board on January 24, 2012.